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Case Report

Acute coronary syndrome in a patient with multifocal coronary vasospasm

Inês Rangel (MD)*, Rui Almeida (MD), Teresa Pinho (MD), Carla de Sousa (MD), Domingos Magalhães (MD), Maria Júlia Maciel (MD, PhD)

Cardiology Department, Centro Hospitalar de S. João, Porto, Portugal

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ABSTRACT

Vasospastic angina results from temporary spasm of one or more coronary segments. Although prognosis of patients presenting with coronary vasospasm appears to be generally good, multivessel coronary vasospasm may increase the risk of life-threatening cardiac events.

We present a case of a 51-year-old man admitted to the emergency room due to severe retrosternal pain, who was documented with multifocal coronary vasospasm.

<**Learning objective:** The case described illustrates the importance of recognizing coronary vasospasm as a cause of reversible ischemia. Although vasospastic angina is associated with a favorable prognosis, multivessel involvement may increase the risk of life-threatening cardiac events.>

Introduction

Vasospastic angina results from temporary spasm of one or more coronary segments and it may be associated with other vasomotor disturbances, such as migraine or Raynaud's phenomenon, suggesting that it may be part of a generalized vascular disorder.

Furthermore, coronary vasospasm and coronary atherosclerotic disease often coexist and may make a mutual contribution to disease progression [1,2].

Acute coronary syndrome (ACS) patients with coronary spasm generally have a good prognosis [3]. However, spontaneous simultaneous multivessel coronary artery spasm is an uncommon finding and a major predictor of worse prognosis [4].

Case report

A 51-year-old obese, smoker, Caucasian man, with a medical history of severe migraine headache, was admitted to the emergency room due to severe retrosternal pain, lasting 30 min, which had started in the early morning, at rest. He had a history of moderate alcohol intake and denied illicit drug use. He had no history of cardiovascular events and took no outpatient medication.

A 12-lead electrocardiogram showed sinus bradycardia alternating with junctional rhythm and ST-segment elevation in leads II, III, aVF, and V5–V6 (Fig. 1a). He was medicated with aspirin 250 mg, clopidogrel 600 mg, sublingual nitroglycerin 0.5 mg, and morphine 4 mg, with minimal symptom relief. Urgent coronary angiography revealed severe simultaneous two-vessel coronary stenoses: two stenoses in the circumflex artery and three stenoses in the right coronary artery (Fig. 2, Videos 1 and 2). Intracoronary administration of nitroglycerin led to a significant relief of all coronary lesions (Fig. 3, Videos 3 and 4), leaving a mild lumen narrowing at the location of these lesions. Also, the chest pain and ST segment elevation resolved (Fig. 1b), thereby establishing the diagnosis of vasospastic angina.

There was a non-significant elevation of cardiac biomarkers (maximal troponin I: 0.06 ng/mL). His full blood count and renal profile were within normal limits. However, he was incidentally diagnosed with diabetes mellitus and dyslipidemia through laboratory testing.

Echocardiography showed a preserved biventricular systolic function and no wall motion abnormalities.

Throughout his hospital stay, the patient remained asymptomatic and clinically stable. Continuous electrocardiographic monitoring did not present any abnormality.

He was discharged home 5 days later, on a regimen of amlodipine 10 mg and isosorbide mononitrate 60 mg daily. He was also medicated with aspirin, simvastatin, and metformin for cardiovascular risk factors (CVRF) control. He was advised to stop smoking.

* Corresponding author at: Cardiology Department, Centro Hospitalar de S. João, Alameda Prof. Hernâni Monteiro, 4200-319 Porto, Portugal. Tel.: +351 966462512; fax: +351 225025766.
E-mail address: inesrang@gmail.com (I. Rangel).

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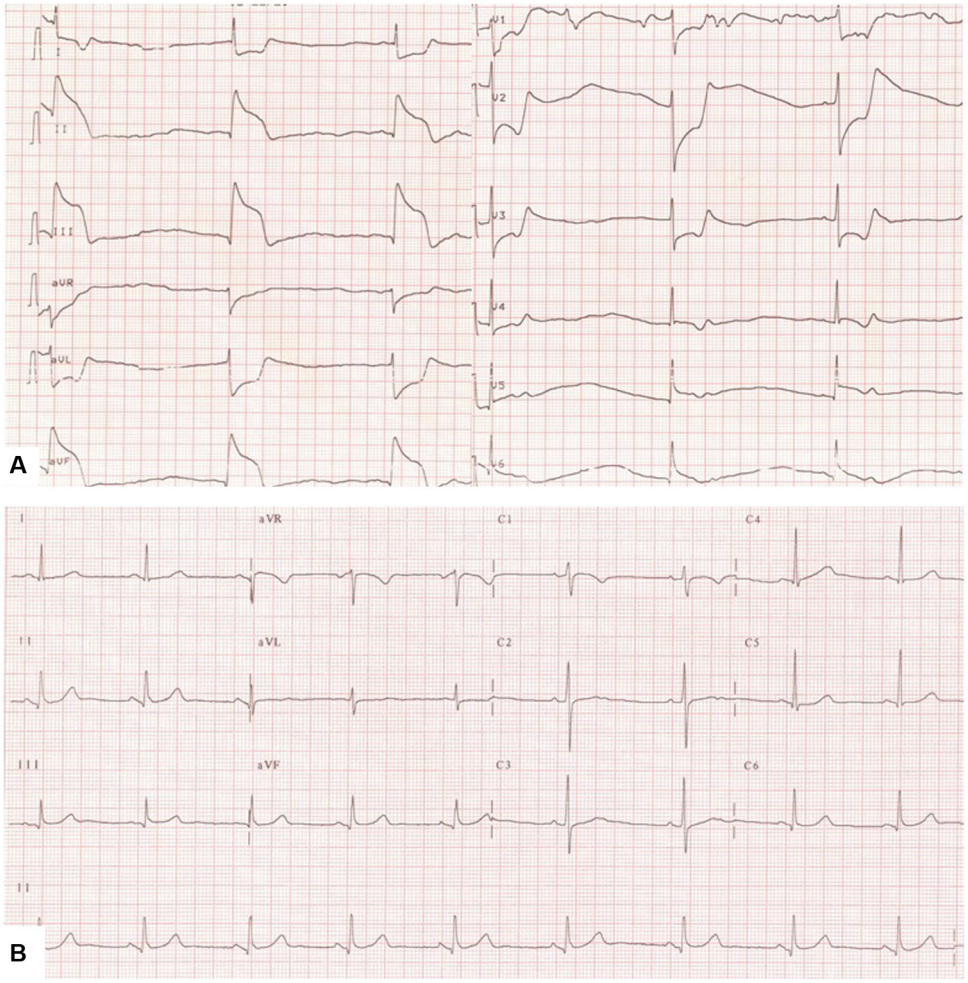

Fig. 1. Electrocardiogram (ECG) on presentation showing ST elevation over inferior and V5–V6 leads (A) and post-catheterization 12-lead ECG showing resolution of ST-segment elevation over inferior and V5–V6 leads (B).

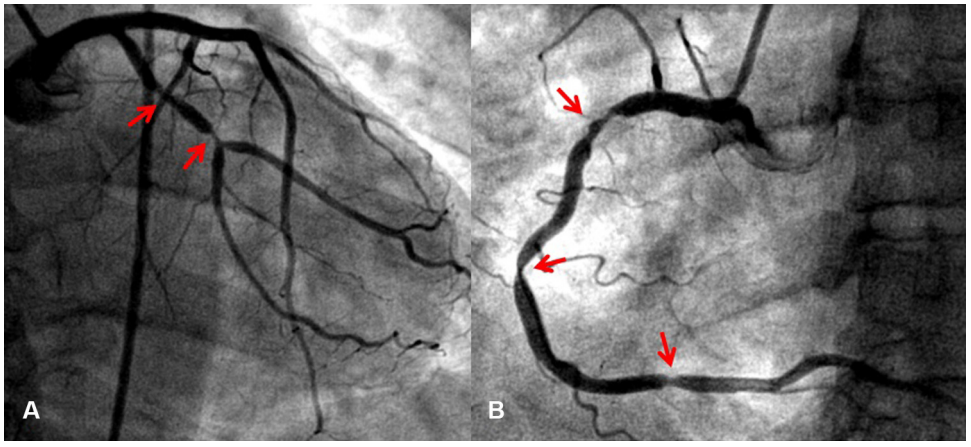

Fig. 2. Angiographic pictures showing multiple stenoses over circumflex artery (A) and right coronary artery (B).

Discussion

Prevalence

Prevalence data of vasospastic angina vary considerably between clinical studies, depending in a large part on the geographic location of the population studied, as well as on the criteria used to test and define the coronary spasm. The CASPAR study reported an estimated coronary spasm prevalence of 12.5% in ACS patients [5].

Yasue et al. [1] suggested that vasospastic angina prevalence has decreased in Europe and North America, possibly due to the lower prevalence of smoking and increased use of calcium-channel blockers.

Vasospastic angina occurs most commonly in middle-aged and older men and post-menopausal women, and is significantly more

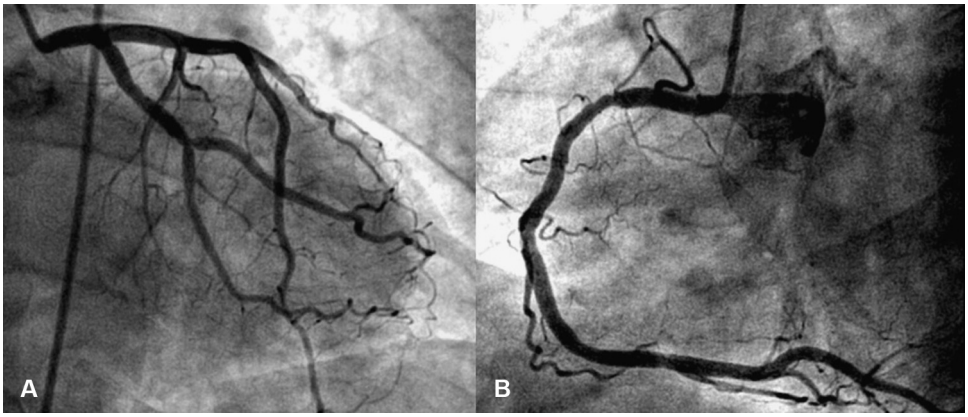

Fig. 3. Normalized circumflex artery (A) and right coronary artery (B) after intracoronary administration of nitrates leading to coronary vasospasm diagnosis.

prevalent in Japanese than Caucasian patients [1]. Pristipino et al. [6] showed that in the early post-myocardial infarction phase, Japanese patients exhibit a 3-fold greater incidence of vasospastic response to intracoronary acetylcholine than Caucasians. This may be related to genetic factors and the high prevalence of smoking in Japanese patients [1]. Because of this high vasospastic angina prevalence, there was a widespread use of calcium-channel blockers in Japanese patients with hypertension and ischemic heart disease, which may have led to a decrease in vasospastic angina in Japan [7].

Pathophysiology and etiology

Vasospastic angina usually occurs at rest, particularly at night and early morning. It is also often induced by mild exercise, during early morning. These circadian variations are possibly due to the autonomic nervous system and hormonal activities [1].

Several mechanisms have been proposed for the pathogenesis of coronary spasm. Oxidative stress-induced endothelial dysfunction is a main factor involved in the pathogenesis of coronary spasm [1]. Then, all the CVRF that are proved to cause endothelial dysfunction may contribute to the occurrence of vasospastic angina. In our case, there were several CVRF (including not previously diagnosed diabetes mellitus and dyslipidemia) that certainly have contributed to the vasospastic event.

Smoking is a crucial risk factor for coronary spasm. Other important risk factors and precipitating factors include alcohol consumption, cocaine abuse, lipid and glucose metabolism abnormalities, magnesium deficiency, and genetic factors [8].

Acute coronary syndrome

Coronary artery spasm is a frequent cause of ACS [5]. The CASPAR study showed that 25% of patients presenting with ACS had no culprit lesion at coronary angiography and nearly 50% of this group of patients had coronary spasm documented by intracoronary provocation with acetylcholine [5]. Vasospastic angina should always be considered as a differential diagnosis in suggestive presentations of ACS, since this clinical entity has a specific therapeutic approach and generally has a good prognosis [3].

Atherosclerosis role

Coronary spasm plays a role in the symptoms of atherosclerotic coronary artery disease including stable angina, ACS and sudden cardiac death [1].

Coronary spasm, which was initially demonstrated in patients with normal or near-normal coronary arteries, frequently develops in sclerotic lesions of varying severity, and is often associated with myocardial ischemia and plaque burden [1,9]. Even when no stenotic lesions are visible on coronary angiography, intravascular ultrasound (IVUS) reveals clear atherosclerotic lesions in locations consistent with regions of coronary spasm [9]. Atherosclerotic disease alters the vasomotor tone and reactivity of the affected vessels, which may lead to a particular susceptibility to coronary spasm events in sites of organic stenosis [1,9]. On the other hand, coronary spasm activates platelets and the coagulation system causing vascular smooth muscle cell proliferation [1]. Ozaki et al. [2] supported the hypothesis that persistent coronary spasm can have a direct role in the process of progression of coronary atherosclerosis as well, as there is an association between cessation of vasospastic angina and regression of atherosclerosis.

Angiographic images of the present case show a significant relief of all coronary lesions after intracoronary administration of nitroglycerin. However, it is possible to verify coronary irregularities in the culprit sites of vasospasm, probably representing subjacent atherosclerotic changes.

Diagnosis

A definite diagnosis of vasospastic angina is based on angiographic demonstration of coronary stenosis during chest pain and/or electrocardiographic changes that resolve spontaneously or after intracoronary infusion of nitroglycerin [8]. Alternatively, a provocative test for coronary spasm can be performed with intracoronary administration of either ergonovine or acetylcholine [1]. It can also be performed with a hyperventilation test, which has a relatively low sensitivity (65%), but a high specificity (100%) [1].

Multivessel disease and prognosis

Patients who present with multivessel vasospastic angina more often have angiographically normal coronary arteries and frequently are resistant to treatment, requiring larger amounts of anti-ischemic medication to suppress symptoms, which often recur on cessation of the drugs [1]. These patients are also more likely to have lethal arrhythmias such as ventricular tachycardia or ventricular fibrillation and are more likely to suffer from sudden death [1,4]. Thus, we may consider that our case carries an inherent worse prognosis due to severe multivessel vasospastic angina.

Treatment

Sublingual nitrates can relieve an attack of vasospastic angina. For the prevention of coronary spasm, treatment with long-acting calcium-channel blockers is the first-line therapy, and additional long-acting nitrates and/or nicorandil are also considered effective

[1,8]. Additional drugs, such as statins, aspirin, angiotensin-converting enzyme inhibitors and angiotensin receptor blockers, may be of benefit [1]. Patients with coronary atherosclerosis should be treated with low doses of aspirin to reduce the risk of cardiovascular events. High doses are not recommended since they may exacerbate coronary spasm by inhibiting the synthesis of prostacyclin, a coronary vasodilator [10].

Patients should control all CVRF, particularly smoking, which may impair endothelial function. Furthermore, patients should avoid excessive alcohol consumption, excessive fatigue, and mental stress [8].

Conclusion

Vasospastic angina should be considered in the presence of ischemia, as it could be reversed with intracoronary nitrates, without the need for coronary stenting.

Although the prognosis of patients presenting with coronary vasospasm appears to be generally good, multivessel coronary vasospasm may increase the risk of life-threatening cardiac events.

Conflict of interest

The authors declare no conflict of interest.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jccase.2014.01.013.

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